D-4. POSSESSION, USE AND TRANSFER OF REGULATED BIOLOGICAL AGENTS

I. INTRODUCTION

In the performance of scientific research, the NCI-Frederick may have occasion to use Select Agents as defined by 42 CFR §73, or High Consequence Animal or Plant Pathogens and Toxins as defined by 9 CFR §121 and 7 CFR §331. It is the policy of the NCI-Frederick to ensure that receipt, usage; storage, shipping and disposal of this material are performed in compliance with all applicable federal and state regulations and laws.

II. SCOPE

All on-site and off-site laboratories of NCI-Frederick receiving, using and transferring regulated biological agents as defined in 42 CFR §73, 9 CFR §121 or 7 CFR §331 will comply with the requirements set forth in this chapter.

III. DEFINITIONS

Biological Agent – Any microorganism or infectious substance, or any naturally occurring, bioengineered, or synthesized component of any such microorganism or infectious substance, capable of causing:

- Death, disease or other biological malfunction in a human, a animal, a plant, or another living organism
- Deterioration of food, water, equipment, supplies, or material of any kind
- Deleterious alteration of the environment

EA-101 Form - CDC form which documents interfacility transfers of Select Agents or CDC/USDA overlap agents.

USDA Form 2041 – USDA form that documents the interfacility transfer of USDA High Consequence Plant & Animal Pathogens and toxins. May also be used to document the interfacility transfer of CDC/USDA overlap agents.

Facility - Any individual or government agency, university, corporation, company, partnership, society, association, firm, or other legal entity located at a single geographic site that may transfer or receive through any means a regulated biological agent subject to 42 CFR §73, 9 CFR §121 or 7 CFR §331. Facility for the purpose of this chapter is the geographical and organizational confines of the NCI-Frederick.

HHS Select Agent - a biological agent or toxin included in 42 CFR § 73.4.

HHS/USDA Overlap Agent - Any microorganism or toxin that poses a risk to both humans and animal health and that is listed in 42 CFR §73.5 or 9 CFR §121.3(b).

Interfacility Transfer - The conveyance or movement from point of origin to a point of destination either from one state or territory to another entirely within one contiguous state or territory, or from one registered facility to another registered facility.

Intrafacility Transfer - a transfer of a Select Agent within the geographic and organizational confines of NCI-Frederick. Transfers of CDC select agents or USDA high consequence pathogen or toxin to other agencies located at Ft. Detrick (i.e., USAMRIID) are not intrafacility transfers.

Requestor - Any individual who receives or seeks to receive through any means a CDC select agent or USDA high consequence pathogen or toxin from any other person or institution.

Responsible Official (RO) - An official authorized to transfer and receive regulated biological agents covered by 42 CFR 73, 9 CFR 121 and 7 CFR 331, on behalf of the transferor and/or requestors facility. The Biological Safety Officer is listed as the "Responsible Official" on the NCI-Frederick Registration Document that was submitted to the regulatory agencies and has been granted the authority and control to ensure compliance with applicable regulations. **The Biological Safety Officer or designee is the individual at the NCI-Frederick authorized to approve the transfer and use of regulated biological agents on behalf of NCI-Frederick researchers.** In the case that the Biosafety Officer is not readily available due to absence from the facility, at least one other EHS staff member has been registered with the regulatory agency as alternate responsible official of record for this facility.

Transferor - Any person who transfers or seeks to transfer through any means a Select Agent to any other person.

USDA High Consequence Pathogen or Toxin – A microorganism or toxin listed in 7 CFR 331.3 or 9 CFR 121.3 that poses a risk to either animals or plants.

IV. PROCEDURE

The Environment, Heath and Safety Program (EHS) has obtained and maintains the NCI-Frederick Registration granted by the U.S. Department of Agriculture (U.S.D.A.) and/or the Centers of Disease Control and Prevention (CDC) as applicable. The NCI-Frederick RO and the NCI-Frederick Institutional Biosafety Committee (IBC) must approve the use of regulated biological agents before a request for procurement is granted.

A. Procurement Of Regulated Biological Agents

1. The procurement of all regulated biological agents will be accomplished only with the documented approval of the RO or alternate, the NCI-Frederick Institutional Biosafety Committee. The list of CDC and USDA regulated agents is attached to this document in Appendix D-4-A.

2. An NCI-Frederick employee who is requesting to obtain a CDC select agent, overlap agent or USDA High Consequence agent, shall contact the NCI-Frederick Biological Safety Officer. Requirements for receiving regulated biological agents or toxins will be discussed at that time.

   Requirements for receiving a CDC/USDA regulated agent may include:

   a. Registration of proposed work with the agent with EHS and the NCI-Frederick IBC via the Pathogen Registration and/or rDNA Registration Programs. Refer to Chapters C-3 and C-5.

b. Inspection of laboratory facilities.

c. Review of research protocol and SOPs.

d. Method of storage and disposal of material when the work has been completed.

e. A list of staff involved with the project will be submitted. These individuals shall comply with the NCI-Frederick biosecurity plan and obtain any and all necessary clearances prior to working with regulated agents. A review of training records of cleared laboratory staff will be conducted to ensure proficiency of individuals working with regulated agents.

f. Once approved at NCI-Frederick, the NIH Select Agent Program Manager will be notified.

g. The RO and the PI will provide all necessary information to the relevant regulatory agencies to request registration or amend a current registration.

Additional information concerning the procedure for the procurement of regulated biological agents and toxins is available from the Biological Safety Officer.

3. CDC select agents, CDC/USDA overlap agents and USDA high consequence pathogens and toxins arriving at NCI-Frederick shall be delivered to the Biosafety Officer or Designee at Building 426, Rm. 136. The Biosafety Officer or Designee shall accomplish final delivery after reviewing the associated documentation and checking the contents. If packages arrive mistakenly at Receiving and Delivery (Bldg. 1050), the biosafety officer shall be notified immediately by the Logistics and Support Manager or designee, and the select agent material will be picked up by the Biosafety Officer or designee, who will accomplish final delivery after a check of contents and review of documentation. Transfers from USAMRIID may be delivered directly to the registered Principal Investigator's laboratory with the documented approval of the Biosafety Officer or the alternate Responsible Official.

B. Regulated Agent Inventory and Shipment

1. The registered principal Investigator shall maintain an inventory of regulated agents in their possession for control purposes. EHS and the RFO reserves the right to request periodic reports concerning the use and location of regulated biological agents.

2. Each Principal Investigator shall keep accurate records of receipt, expenditure, and relocation of the regulated agents for which he/she is responsible. Principal Investigator(s)/Area Supervisor(s) will utilize the NIH Select Agent Log (Appendix D-4-B) sheet to maintain inventory records. Intrafacility transfer records shall include the name and location of the recipient; the amount of agent transferred,

the date of transfer, the intended use of agent.

3. Intrafacility transfer records must be maintained for a period of five years after the date of transfer or for five years after the agents are spent or properly disposed, whichever is longer. **Intrafacility transfer of regulated agents requires documented approval by the Biological Safety Officer or Alternate RO**. All requests for Intra-facility transfer of regulated agents must be documented on the attached request form (Appendix D-4-C) and submitted to EHS 24-hours prior to the Intra-facility transfer. Transfer of any amount of regulated agents to unauthorized areas is **prohibited**. EHS reserves the right to periodically audit all inventory, intrafacility transfer records and other related records kept by the P.I./Lab Chief/Lab Manager.

4. Interfacility shipments of regulated agents from NCI-Frederick to other destinations **must be cleared in advance** through the Biological Safety Officer to assure conformance with Health & Human Services (42 CFR 73), USDA (9 CFR 121 and 7 CFR 331), Department of Transportation, Postal, and other shipping regulations. The CDC EA101 or USDA Form 2041 will be completed and faxed to CDC or the USDA as appropriate for approval. Only after regulatory agency has provided the approval confirmation number will the material be shipped to the requesting facility.

5. When transferring a regulated agent, researchers shall provide a Request for Shipment form to Transportation and EHS **48 hours** in advance for all pre-approved shipments of regulated agents.

    a. A copy of the completed form shall be faxed to CDC and NCI-Frederick Biosafety Officer or designee by the requesting facility, when the transfer of materials has taken place.

V. RESPONSIBILITIES

A. Purchasing Department:

1. Ensures that the Biosafety Officer or Alternate Responsible Official has previously approved purchase requests for select agent materials prior to placing an order with a vendor.

2. Instructs the vendor to deliver select agent material to only the Biosafety Officer or designee at Building 426, Rm. 136

B. Environment, Health and Safety Program:

1. Through its regulatory and auditing role, ensures that the receipt, storage, and issue of regulated biological agents at the NCI-Frederick are in compliance with federal and state regulations.

2. Provides assistance to laboratory personnel on inventory control procedures, secure storage, and proper disposal of regulated biological agents.

3. Maintains records (CDC Form EA-101/USDA Form 2041) on all interfacility transfers of CDC select agents, CDC/USDA overlap agents and USDA high consequence animal & plant agents at the NCI-Frederick. Records of interfacility transfers are retained for a period of five years after the date of shipment or for five years after the regulated agent(s) are spent or properly disposed, whichever is longer.

4. Maintains the NCI-Frederick Agent Registration issued by USDA and/or CDC. EHS will provide CDC/USDA updated information on any additions, deletions, or changes to the NCI-Frederick Registration.

C. NCI-Frederick Investigators (includes government and contractor investigators)

1. Review, confirm, and communicate to staff the requirements for working with regulated biological agents in laboratories for which they are responsible.

2. Control access to laboratories for which they are responsible and restrict access to regulated agents to only those individuals that have obtained the necessary clearance and training to work with research material regulated by 42 CFR 73, 9 CFR 121 and 7 CFR 331.

3. Maintain accurate records of receipt, expenditure, relocation and disposal of regulated biological agents for which they are responsible.

4. Forward information regarding method and date of agent disposal to the responsible official (RO).

5. Store, use, and dispose of regulated biological agents in compliance with relevant regulations and NCI-Frederick policy.

HHS Select Agents, and USDA High Consequence Livestock & Plant Pathogens or Toxins

Viruses

1. African horse sickness virus
2. African swine fever virus
3. Akabane virus
4. Avian influenza virus (highly pathogenic)
5. Blue tongue virus (exotic)
6. Camel pox virus
7. Cercopithecine herpes virus (Herpes B virus)
8. Classical swine fever virus
9. Crimean-Congo haemorrhagic fever virus
10. Eastern equine encephalitis virus
11. Ebola viruses
12. Foot and mouth disease virus
13. Goat pox virus
14. Japanese encephalitis virus
15. Lassa fever virus
16. Lumpy skin disease virus
17. Malignant catarrhal fever
18. Marburg virus
19. Menangle virus
20. Monkeypox virus
21. Newcastle disease virus (exotic)
22. Nipah and Hendra complex viruses
23. Peste des petits ruminants
24. Plum pox potyvirus
25. Rift Valley fever virus
26. Rinderpest virus
27. Sheep pox
28. South American haemorrhagic fever viruses [(Junin, Machupo, Sabia, Flexal, Guanarito)]
29. Swine vesicular disease virus
30. Tick-borne encephalitis complex (flavi) viruses [Central European Tick-borne encephalitis, Far Eastern Tick-borne encephalitis (Russian Spring and Summer encephalitis, Kyasanur Forest disease, Omsk Hemorrhagic Fever)]
31. Variola major virus (Smallpox virus) and Variola minor (Alastrim)
32. Venezuelan equine encephalitis virus
33. Vesicular stomatitis virus (exotic)

Prion

1. Bovine spongiform encephalopathy agent

Toxins

1. Abrin
2. Botulinum neurotoxins
3. *Clostridium perfringens* epsilon toxin
4. Conotoxins
5. Diacetoxyscirpenol
6. Ricin
7. Saxitoxin
8. Shigatoxin and Shiga-like ribosome inactivating proteins
9. Staphylococcal enterotoxins
10. Tetrodotoxin
11. T– 2 toxin

Bacteria

1. *Bacillus anthracis*
2. Botulinum neurotoxin producing strains of *Clostridium*
3. *Brucella abortus*
4. *Brucella melitensis*
5. *Brucella suis*
6. *Burkholderia mallei*
7. *Burkholderia pseudomallei*
8. *Coxiella burnetii*
9. *Cowdria Ruminantium* (Heartwater)
10. *Francisella tularensis*
11. *Liberobacter africanus, Liberobacter asiaticus*
12. *Mycoplasma capricolu/M.* F38/*M. mycoides capri* (contagious caprine pleuropneumonia agent)
13. *Mycoplasma mycoides mycoides* (contagious bovine pleuropneumonia agent)
14. *Ralstonia solanacearum* Race 3
15. *Rickettsia prowazekii*$^{\Psi}$
16. *Rickettsia rickettsii*
17. *Xanthomonas oryzae* pv. oryzicola
18. *Xylella fastidiosa* (citrus variegated chlorosis strain)
19. *Yersinia pestis*

Fungi

1. *Coccidioides immitis*
2. *Coccidioides posadasii*
3. *Peronosclerospora philippinensis*
4. *Phakopsora pachyrhizi*
5. *Sclerophthora rayssiae var zeae*
6. *Synchytrium endobioticum*

Exemptions

The following agents or toxins are exempt if the aggregate amount under the control of a principal investigator does not, at any time, exceed:

- 0.5 mg of Botulinum neurotoxins
- 5 mg of *Staphylococcal* enterotoxins
- 100 mg of abrin, *Clostridium perfringens* epsilon toxin, conotoxin, ricin, saxitoxin, shigatoxin, shiga-like ribosome inactivating protein, and tetrodotoxin
- 1,000 mg of diacetoxyscirpenol and T-2 toxin

The following agents or toxins are also exempt:

- Any agent or toxin that is in its naturally occurring environment provided it has not been intentionally introduced, cultivated, collected, or otherwise extracted from its natural source.
- Non-viable select agent organisms or nonfunctional toxins.
- The vaccine strains of Junin virus (Candid #1), Rift Valley fever virus (MP-12), Venezuelan Equine encephalitis virus vaccine strain TC-83.
- The medical use of toxins for patient treatment is exempt.

Genetic Elements, Recombinant Nucleic Acids, and Recombinant Organisms

1. Select agent viral nucleic acids (synthetic or naturally derived, contiguous or fragmented, in host chromosomes or in expression vectors) that can encode infectious and/or replication competent forms of any of the select agent viruses.
2. Nucleic acids (synthetic or naturally derived) that encode for the functional form(s) of any of the listed toxins if the nucleic acids: a) are in a vector or host chromosome; b) can be expressed *in vivo* or *in vitro*; or c) are in a vector or host chromosome and can be expressed *in vivo* or *in vitro*.
3. Listed viruses, bacteria, fungi, and toxins that have been genetically modified.

Other Restrictions

1. Experiments utilizing recombinant DNA that involve the deliberate transfer of a drug resistance trait to the listed agents that are not known to acquire the trait naturally, if such acquisition could compromise the use of the drug to control disease agents in humans, veterinary medicine, or agriculture.
2. Experiments involving the deliberate formation of recombinant DNA containing genes for the biosynthesis of listed toxins lethal for vertebrates at an LD50 < 100 ng/kg body weight.

APPENDIX D-4-B

CDC Select/USDA High Consequence Agent Logbook

Principal Investigator: _____

Biological Agent : __ _____

Storage Lab Building/Room: _____

Date of Receipt	Initials of Receiver		Quantity	Number of Vials /Containers

Date	Initials	Generation/Use/Dispose (indicate appropriate action)	Quantity	Number of Vials
TOTAL				
TOTAL				
TOTAL				
TOTAL				
TOTAL				
TOTAL				
TOTAL				
TOTAL				

APPENDIX D-4-C
INTRA FACILITY TRANSFER REQUEST

For the approval of INTRA FACILITY Select Agent Transfers, please forward transfer request with all pertinent information to the Biological Safety Officer / Safety Environmental Protection Program, building 426 room 118, no less than 24 hours prior to the desired transfer date.

AGENT INFORMATION

Agent Name

Of Primary Containers to be transferred _____ Volume Per Container

TRANSFEROR INFORMATION

Date Of Request _____ Date Of Requested Transfer

Transferor Name _____ Work Phone

Program / Dept.

Reason For Transfer Request

Transferor Signature _____ Date

RECIPIENT INFORMATION
(Upon consumption of select agent materials it is the responsibility of the recipient to forward to the Biological Safety Officer information regarding the method and date of select agent disposal)

Recipient Name _____ Work Phone

Program / Dept.

Location of Select Agent Use and Storage: Building _____ Room

BioSafety Level of Receiving Laboratory: BL-2 _____ BL-3 _____ Other

Method of Disposal _____ Date of Disposal

TRANSFER AUTHORIZATION (EHS USE ONLY)

APPROVED _____ **NOT APPROVED** _____

Comments:

_____ Date _____ **Tracking ID** _____
EHS Authorized Individual